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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/163,089	09/29/1998	IAN F. C. MCKENZIE	5036-1	9586

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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 04/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/163,089	**Applicant(s)** MCKENZIE ET AL.	
	Examiner Robert A. Zeman	**Art Unit** 1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 October 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *see attached*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): none.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,3-17,19-21,24-26,38 and 70-72*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached..
12. ☒ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). 11-12-2004
13. ☐ Other: _____.

ADVISORY ACTION

The period for reply is extended to run 6 MONTHS from the date of the final rejection. Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a) accompanied by the appropriate fee. The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. A reply within the meaning of 37 CFR 1.113 or a request for a continued examination (RCE) in compliance with 37 CFR 1.114 must be timely filed to avoid abandonment of this application.

The amendment filed 10-27-2004 under 37 CFR 1.116 in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance and will not be entered because: minimally the proposed amendment raises new issues under 35 U.S.C. 112, first paragraph.

The Declaration filed on 10-27-2004 will not be considered because good and sufficient reasons why it was not earlier presented have not been shown. Applicant's assertion that said Declaration is timely since it was submitted only to clarify issues raised by the Examiner has been fully considered and deemed non-persuasive. The aforementioned Declaration includes data that should have been submitted in response to the rejections set forth in the Office action mailed 4-26-2004.

Since Applicant's arguments are predicated on an amendment and Declaration not of record, said arguments are deemed non-persuasive. Consequently, all pending rejections are maintained for reasons of record and are reiterated below.

Claim Objections Maintained

The objection to claim 71 under 37 CFR 1.75 as being a substantial duplicate of claim 70 is maintained for reasons of record. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Mannan is a polymer of mannose.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-17, 19-21, 24-26, 38 and 70-72 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the previous Office action in the rejection of claims 1, 3-17, 19-21, 24-26, 38 and 70. The specification, while being enabling for immunoregulatory compositions comprising mannose receptor bearing cells, and a conjugate comprising MUC1 (antigen) and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes, does not reasonably provide enablement for immunoregulatory compositions comprising mannose bearing cells and a conjugate comprising any antigen and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized polymer comprising free aldehydes.

Applicant argues:

1. Applicants have provided evidence that at least two different antigens can be used with the claimed conjugate and composition which, when administered *in vivo* to an animal, elicits an antigen specific immune response.

2. The mechanism of enhancing the immune response is provided by the constant factors in the composition of the mannose receptor bearing cells and the oxidized carbohydrate polymer not the specific antigen.

3. The data of Davis et al. supports the predictability of the use of the claimed composition with any suitable immunizing agent.

4. Applicants are in the process of preparing additional data showing the use of the instant invention comprising yet another antigen.

5. Applicant's have demonstrated that at least two different cell types can be successfully used in the composition of the invention.

6. Applicants submit that any mannose receptor bearing cells that are capable of delivering an antigen to the MHC class I pathway for MHC class I antigen presentation will be suitable for use in the instant invention.

7. The composition comprising CRIPTO and dendritic cells (as disclosed in the declaration of Dr. Pietersz) was administered to mice *in vivo* and hence demonstrated its *in vivo* efficacy.

8. Since the Declaration by Dr. Pietersz states that the conjugate of manna-Cripto was "prepared as described in the present application", it was assumed that it would be understood that the mannan was fully oxidized since oxidized mannan was disclosed in the instant specification.

Applicant's arguments have been fully considered and deemed non-persuasive.

The instant invention is drawn to compositions comprising isolated mannose receptor-bearing cells **and** a conjugate comprising an antigen and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes. **The mannose receptor-bearing cells are a required component** of said composition.

With regard to Points 1-3 and Point 7, Applicant's arguments, as well as the paper by Davis et al., demonstrate the effects of the antigen-polymer conjugate only. Davis et al. disclose the *ex vivo* pulsing of macrophage cultures and the measurement (profiling) of cytokine production. The compositions of Davis et al. are not commensurate in scope with the instant invention since they utilize only an antigen-polymer conjugate. As stated previously, the mannose receptor-bearing cells are a required component of the claimed invention. Therefore, since Applicant's arguments do not address compositions that fall within the metes and bounds of the rejected claims, they are deemed non-persuasive. Moreover, the data presented in the Declaration by Dr. Pietersz is not representative of the full scope of the claims. Said data demonstrated the *ex vivo* pulsing of a single cell type (dendritic cells) utilizing a single antigen (CRIPTO) and the ability of splenocytes taken from mice immunized with said pulsed cells to produce KIFN in an *in vitro* assay. Said data is not commensurate in scope with the claimed invention since the antigen-polymer conjugate was removed from the pulsed dendritic cells prior to administration to the mice (see page 2 of Declaration).

With regard to Point 4, since no data was provided in a timely manner, Applicant's assertion regarding what said data demonstrates is given no weight.

In response to Point 6, it is noted that the features upon which applicant relies (i.e., that the mannose receptor bearing cells must be capable of MHC class I antigen presentation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With regard to Point 8, since the specification discloses conjugates comprising fully oxidized mannose or partially reduced mannose. Consequently, one could not conclude that the conjugate utilized by Dr. Pietersz was commensurate in scope to the instant invention based on the statement that "manna-Cripto was prepared as described in the present application".

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Zeman
March 28, 2005

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